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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/598,698 | HELLERBRAND ET AL. | |
| | Examiner | Art Unit | |
| | DENNIS HEYER | 1628 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *19 July 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

5)☒ Claim(s) *1, 4, 6, 8 – 9, 11 – 17, 48 and 51 – 54* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1, 4, 6, 8 – 9, 11 – 17, 48 and 51 – 54* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Acknowledgement is made of Applicant's remarks and amendments filed July 19, 2011. Acknowledgement is made of the amendment to independent method Claim 1 which now recites the limitations to method step (a) "providing a container having a receptacle for receiving the device to be coated, wherein the receptacle of the container is coaxially located within a container housing, the container and the receptacle being configured so that the device is coatable with the coating substance directly in the container, wherein an inner surface of the receptacle is coated with a layer of an inert, repelling material configured to increase a quantitative deposition of the coating substance on the device". Acknowledgement is made of the addition of new Claim 54 which recites the methods steps of amended Claim 1 and the limitation of Claim 11.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

### *Status of Claims*

Claims 1, 4, 6, 8 – 9, 11 – 17, 48 and 51 – 54 are currently pending.

## ***Withdrawn Rejections***

***Claim rejections – 35 USC § 103***

The rejection of Claims 1, 4, 6, 8, 11 – 12 and 16 – 17 under 35 U.S.C. 103(a) as being unpatentable over Song in WO 2005/016399 in view of Talalay in US patent 4,063,367 and Graff, D.A. in US Patent 5,316,146 is rendered moot and is withdrawn in response to Applicant's amendment to Claim 1 requiring in the claimed method that the container and the receptacle are "configured so that the device is coatable with the coating substance directly in the container" and, "wherein an inner surface of the receptacle is coated with a layer of an inert, repelling material configured to increase a quantitative deposition of the coating substance on the device". Neither the Song, Talalay nor Graf references teach an inner surface of a receptacle coated with a layer of an inert, repelling material

The rejection of Claims 9, 13, 48 and 52 – 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Song in WO 2005/016399 in view of Talalay in US patent 4,063,367 and Graff, D.A. in US Patent 5,316,146 and further in view of Kohnert *et al.* in WO 2003/043673 is rendered moot and is withdrawn in response to Applicant's amendment to Claim 1.

The rejection of Claim 15 under 35 U.S.C. 103(a) as being unpatentable over Song in WO 2005/016399 in view of Talalay in US patent 4,063,367 and Graff, D.A. in

US Patent 5,316,146 and further in view of Lee *et al.* in US patent 5,571,523 is rendered moot and is withdrawn in response to Applicant's amendment to Claim 1.

The rejection of Claim 51 under 35 U.S.C. 103(a) as being unpatentable over Song in WO 2005/016399 in view of Talalay in US patent 4,063,367 and Graff, D.A. in US Patent 5,316,146 and further in view of Gao *et al.* in US patent 6,113,993 is rendered moot and is withdrawn in response to Applicant's amendment to Claim 1.

## ***New Rejections***

*It is noted that the Song, Talalay, Graf, Kohnert, Lee and Gao references were previously applied in the Office Action mailed April 20, 2011. The Klokkers-Bethke reference was previously applied in the Office Action mailed November 27, 2009, withdrawn in the Office Action mailed March 17, 2010 and reapplied in the instant Office Action as necessitated by the amendment to instant Claim 1 and new Claim 54.*

### ***Claim rejections – 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 1, 4, 6, 8, 11 – 12, 16 – 17 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Song in WO 2005/016399 (priority date: August 11, 2004, published: February 24, 2005) in view of Klokkers-Bethke *et al.* in US Patent 5,335,769, Talalay in US patent 4,063,367 (published: December 20, 1977) and Graff, D.A. in US Patent 5,316,146 (published: May 31, 1994).**

*This new ground of rejection is necessitated by Applicant's amendment to Claim 1 and the addition of new independent Claim 54.*

Song teaches a medical device comprising a substrate, a therapeutic agent containing region over the substrate which comprises a therapeutic agent and an antioxidant (a coating) as well as methods of making said coated devices (Abstract).

Song teaches providing a solution comprising a solvent, a therapeutic agent and an antioxidant, contacting the solution with a medical device substrate and then removing the solvent from the solution to form a therapeutic-agent-containing region (Abstract; instant Claim 4). Song teaches 'dipping techniques' (i.e. inserting the device into a solution) as a preferred solvent-based technique for contacting the device with a solution (p [0042]; instant Claim 1, step c).

The teaching of "dipping" to coat a medical device with a therapeutic agent-containing solution is reasonably construed by one of ordinary skill in the art as teaching the method steps (a) and (b) of instant Claim 1 drawn to providing the required receptacle, and the solution within said receptacle in order that the medical device can be dipped (i.e. coated, Claim 1, step c). Further, coating a device by dipping into a receptacle (a container) containing a solution comprising a therapeutic agent, is reasonably construed as "the receptacle being configured so that the device is coatable with the coating substance directly in the container" as required by amended Claim 1. It is noted that although Song does not explicitly recite the term receptacle, the technique of "dipping" a medical device into a liquid solution clearly requires that said solution be "contained". Accordingly, the solution of Song is reasonably construed as being *present within a receptacle* thus meeting the limitation of the "providing" and "inserting" steps (b) and (c) recited in instant Claim 1.

Instant Claim 6 is drawn to immobilization of the pharmaceutically active substance to an inorganic or organic bioresorbable material. Song teaches that the process of contacting a substrate containing a previously formed polymer layer with a solution containing a therapeutic agent (pharmaceutically active substance) results in said agent being "imbibed by the polymer" (p [0044]). One of ordinary skill would reasonably construe the process of "imbibing" (defined as: to take in, absorb) to meet the limitation of 'immobilized' as defined in p [0053] of the instant specification. Song also teaches that the imbibing (immobilization) may occur within a bioresorbable material including polypeptide biopolymers as coatings (p [0039]).

Song teaches the solution contacting the medical device comprises non-active ingredients, specifically, a polystyrene-polyisobutylene block copolymer (page 13, Example 3, paragraph [0050]; instant Claim 8). Song teaches the solution contacting the medical device is an organic solvent, tetrahydrofuran (page 13, Example 3, paragraph [0050]; instant Claim 12). Song teaches the solution contacting the medical device contains an antioxidant, said antioxidant comprising BHT, BHA or tocopherol (Abstract, step a (iii), paragraph [0009], see also, page 13, Example, paragraph [0050]; instant Claim 14). Song teaches that the medical device may be a stent (page 13, Example 3, paragraph [0050]) and that the medical device includes any coated substrate which can comprise, for example, metal (page 3 – 4, paragraph [0020]) (instant Claims 16 and 17).

As discussed above, Song teaches the step of drying (i.e. removing volatile components from) a coated medical device in an oven after removing the device from the solution into which it had been dipped. Song does not teach drying the device by "starting isothermal drying of the device while the device remains held within the solution held within the container, thereby removing the volatile components from the solution of the coating substance" as required by Claim 1, step (d).

Song also does not explicitly teach the limitation in Claim 1, step (a), which requires that the receptacle into which the medical device is dipped (inserted) is coaxially located within a container housing, the limitation of amended Claim 1 method step (a) "wherein the inner surface of the receptacle is coated with a layer of an inert, repelling material, configured to increase a quantitative deposition of the coating

substance on the device" or, the method recited in instant Claims 11 and 54 "wherein the container becomes a packaging container for the device".

Klokkers-Bethke *et al.* teach a method for packaging lyophilizates in glass containers (i.e. a receptacle, e.g. vials ampoules and bottles) that become the packaging container (i.e. the "primary packaging means", column 1, lines 9 – 10; instant Claims 11 and 54).

Klokkers-Bethke teaches that moisture sensitive medicinal substances must be stabilized for storage and that a customary stabilizing method is to dry a solution of said substance by removing the solvent by lyophilization (column 1, lines 17 – 21).

Klokkers-Bethke teaches that glass containers (receptacles), e.g. ampoules, made of Type-I glass create manufacturing problems and product loss because the product cake formed in the receptacle following freeze-drying lacks coherence and has too little physical stability which leads to distribution of the lyophilizate throughout the entire container (receptacle). Klokkers-Bethke teaches said product loss increases production costs when ampoules are used and unpredictably reduces product storage stability when vials or bottles having puncturable caps are used (column 3, lines 42 – 52).

Klokkers-Bethke teaches that coating the inside surface of a glass container (receptacle) with a silicone material substantially eliminates the above-mentioned manufacturing problems and product deficiencies (column 3, lines 51 – 55).

Klokkers-Bethke teaches a method of freeze-drying (i.e. removing volatile components from the solution of the coating substance; Claim 1, step d) which reduces

loss of the freeze-dried product, said method comprising 1) adding a liquid solution comprising $PGE_1$ (a pharmaceutically active solid product), lactose and $\alpha$-cyclodextrin dissolved in a solvent to a glass container (receptacle) having its inside surface coated with a silicone material (as evidenced by page 24, lines 4 – 6 of the present specification, silicone is an inert, repelling material; amended instant Claim 1, step d), 2) starting freeze-drying, under a nitrogen atmosphere, of said liquid solution in said receptacle, to remove volatile components and provide said solid product in the receptacle in the form of a dense compact coherent solid; 3) further drying the coherent solid product under a nitrogen atmosphere at a vacuum of $10^{-3}$ mbar and, 4) sealing the container in order to maintain a stable solid product over a useful storage shelf life (Abstract; Example, column 4, lines 28 – 50). Accordingly, Klokkers-Bethke teaches removing volatile substances from the solution containing a therapeutic agent by lyophilization in which a therapeutic substance, PGE1, remains within the solution held within a glass container that becomes the packaging container (instant Claim 1, step (d) and instant Claims 11 and 54).

The teaching of Klokkers-Bethke of obtaining a dense compact solid (which prevents a loss of 10% of the lyophilized product) by coating the inner surface of the container (receptacle) with silicone is construed as meeting the functional limitation recited in amended Claim 1 "increasing a quantitative deposition of the coating surface on the device" because one of ordinary skill would reasonably construe the formation of a dense compact solid as minimizing the 'distribution of the lyophilizate throughout the entire container' which is observed for receptacles that lack a silicon coating.

Klokkers-Bethke teaches removing the solvent (volatile components) by freeze-drying such that the container (i.e. the receptacle) that is subject to lyophilization becomes the packaging container but does not explicitly teach removing the solvent (the volatile components) by isothermal drying as recited in instant Claim 1, step (d).

Klokkers-Bethke also does not explicitly teach the limitation in Claim 1, step (a), which requires that the receptacle is coaxially located within a container housing.

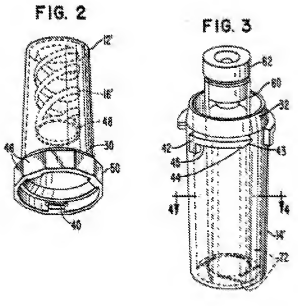
Talalay teaches a method for drying liquid contained in a receptacle comprising a biologically active liquid solid composite comprising the step of passing a stream of dry air over said container in order to evaporate the liquid from said container (Claims 1 and 3). Talalay does not use the term 'isothermal drying', however, Talalay teaches a process in which the temperature is held constant (column 3, lines 56 – 58) and thus the drying process of Talalay is considered to fall within the scope of the process of 'isothermal drying' disclosed on page 20, lines 7 – 25 of the present specification. Talalay teaches the receptacles are subsequently subjected to a vacuum to complete the drying operation (removal of liquid), filled with an inert gas and then sealed (column 2, lines 2 – 7; see also Claims 3 and 4). Talalay teaches that the process of drying the biologically active material and sealing the receptacles ensures a long shelf life removes residual moisture from the containers as well as oxygen and airborne contaminants (column 2, lines 10 – 13).

Song in combination with Klokkers-Bethke and Talalay teach a method for coating a device, while the device remains in the receptacle, by removing volatile components from the solution of the coating substance by isothermal drying, wherein

the receptacle becomes the packaging container and wherein the inner surface of said receptacle is coated with an inert, repelling material (silicone).

The combination of references do not explicitly teach the limitation of Claim 1, step (a) which requires that the receptacle (which contains the coated device) is located coaxially within a container housing. The combination of references therefore does not teach a container which becomes the packaging container for the device (instant Claim 11) because the term *'packaging container'* requires both the receptacle (which contains the coated device) and a housing, wherein the receptacle is located coaxially within said housing.

Graff teaches a transport container (i.e. a packaging container) for transporting fragile articles such as test tubes or vials in order to protect the contents from impact shocks associated with transport and thus prevent breakage of the vials. (Abstract). Figure 3 (below) of Graff illustrates the coaxial orientation of the vial (a receptacle, element '60') within the container housing (transporter base, element 14').



For further clarity, it is noted that the housing also includes a cap (FIG. 2, element 12') which is placed on top of the base in order to completely encapsulate the vial receptacle contained within the housing.

Graff teaches that the vial transporter (a housing) prevents or minimizes leakage from a vial (a receptacle) during transport and that even if fluid were to leak from the receptacle it would be contained within the transport container (the housing) (column 2, lines 56 – 66). Graff teaches the transporter (a housing) restrains the vial (the receptacle) from moving in the radial and longitudinal directions and away from the walls of the transporter (housing). Thus the housing walls are better able to absorb shocks or impact associated with transport and prevent damage to the receptacle (columns 2 – 3, bridging paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made, to modify the oven drying step taught by Song to alternatively, dry the device by removing volatile components from the solution of the coating substance while the device is held in a coating solution within a receptacle that becomes a packaging container.

One would have been motivated to do so because starting drying by the method of Klokkers-Bethke (i.e. freeze-drying under reduced vacuum in an inert atmosphere) while the device is held in a coating solution within a receptacle followed by sealing said receptacle such that it becomes a packaging container minimizes exposure of the coated device to an oxidizing atmosphere which, as taught by Klokkers-Bethke, provides stability to the dried product allowing for a useful storage shelf life. Further,

Song explicitly teaches the desirability of limiting exposure of the coated medical device to an oxidizing atmosphere by maintaining it in an inert atmosphere ("it may be beneficial to maintain a therapeutic agent coated onto a medical device in a non-oxidizing environment during the course of its formation", Song, page 12, p [0046] and [0047]) *and*, encourages placing the coated medical device into packaging (a receptacle) that has been evacuated or into which an inert gas (e.g. nitrogen) has been introduced in order to maintain a non-oxidizing environment (Song, p [0047]).

Accordingly, modifying the drying (dipping) step of Song such that the solvent is removed while the device remains in the coating solution and wherein receptacle becomes the packaging container by the freeze drying and sealing steps of Klokkers-Bethke, both of which are carried out under vacuum and in a nitrogen atmosphere, would avoid the step of transferring the coated device from a potentially oxidizing atmosphere to a "package" that contains an inert atmosphere.

In addition, it would have been *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made, to modify the method of Song wherein said device remains within the solution held within the receptacle and wherein said receptacle is coated with an inert repelling substance. One would have been motivated to do so because Klokkers-Bethke teaches that coating the inside surface of a glass receptacle with a silicone material (an inert repelling substance) substantially eliminates undesired distribution of the lyophilizate throughout the entire receptacle which decreases production costs by minimizing product loss and increasing product storage stability. Accordingly, one of ordinary skill would have recognized that applying a

silicone coating to the inner surface of the receptacle would increase adherence (i.e. quantitative deposition) to non-silicon treated surfaces (i.e. the medical device of Song) within the receptacle upon removal of the solvent.

Moreover, it would have been *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made, to substitute isothermal drying for removing the volatile components from the coated medical device in the method of Song and Klokkers-Bethke for 'freeze-drying'. One would have been motivated to do so because Talalay teaches isothermal drying allows one to seal the receptacle (container) following removal of moisture (liquid) and thus ensure a longer shelf life of the material contained within. See MPEP 2141; section III, KSR Exemplary Rationale B: Simple substitution of one known element for another to obtain predictable results. In the present case, substituting the known method step of lyophilization (Klokkers-Bethke) to remove volatile components under reduced pressure for the known method of isothermal drying (Talalay) for the predictable result of removing volatile components from the coating solution of Song in a receptacle that becomes a packaging container resulting in an increase in the shelf life of the material contained within.

Finally, it would have been *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made, to modify the receptacle in the method of Song in combination with Klokkers-Bethke and Talalay for coating a medical device with a housing in which the receptacle is located coaxially within said housing. One would have been motivated to do so because Graff teaches that vials (receptacles) contained coaxially within a housing have a reduced risk of breaking and releasing the fluid

contained within during transport because the housing walls can absorb shocks during transport. Accordingly, one would have been motivated to prepare the coated medical device in a receptacle maintained in an inert gas or non-oxidizing environment (Song) to extend its shelf life (Klokkers-Bethke and Talalay) in a packaging container housing wherein the receptacle is located coaxially (Graf), in order to minimize, upon transport of the receptacle, damaging or breaking the receptacle and undesired release of the inert gas (a fluid) contained therein.

**Claims 9, 13, 48 and 52 – 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Song in WO 2005/016399 A1 (priority date: August 11, 2004, published: February 24, 2005) in view of Klokkers-Bethke *et al.* in US Patent 5,335,769, Talalay in US patent 4,063,367 (published: December 20, 1977) and Graff, D.A. in US Patent 5,316,146 (published: May 31, 1994), as applied to Claims 1, 4, 6, 8, 11 – 12, 16 – 17 and 54, and further in view of Kohnert *et al.* in WO 2003/043673 (published: May 30, 2003).**

*This new ground of rejection is necessitated by Applicant's amendment to Claim 1 and the addition of new independent Claim 54.*

As discussed in the 103(a) rejection above, the combination of Song, Talalay and Graff renders obvious the method of coating a device recited in instant Claims 1, 4, 6, 8, 11 – 12, 16 – 17 and 54.

The combination of references do not teach a coating substance comprising calcium phosphates (instant Claim 9), or the device being calcium phosphate or β-tricalcium phosphate (instant Claims 52 – 53). The references also do not teach an

acidic aqueous contacting solution (instant Claim 13), or that the method of instant Claim 1 provides a homogeneous distribution of the coating on the device (instant Claim 48).

Kohnert teaches devices having osteoconductive and osteoinductive properties (Title) comprising a carrier containing calcium phosphate wherein said carrier is homogeneously coated with protein (Abstract). Kohnert teaches a method for preparing said devices comprising providing a solution comprising an osteoinductive protein and a buffer and contacting the solution with a carrier containing calcium phosphate.

Kohnert teaches that the contacting solution comprises a carrier containing calcium phosphate (page 6, 3rd paragraph; instant Claim 9). Kohnert teaches that the device may be made of calcium phosphate or β-tricalcium phosphate (Claim 11, instant Claims 52 and 53). Kohnert teaches that the contacting solution comprises a buffer, and that, preferably, the preferred pH is between 4 and 6 (page 8, paragraphs 3 and 4), which meets the limitation of the instant Claim that the contacting solution be an aqueous acidic solution (instant Claim 13).

Instant Claim 48 is drawn to a homogeneous distribution of the coating on the device. Kohnert teaches a method that provides a homogeneous coating on the surface of the device (page 6, paragraph 3 to page 7, paragraph 1, in particular step (c)) and teaches that an advantage of the present invention is the homogeneous coating which is achieved during the coating process (page 7, paragraph 4).

One would have been motivated to modify the method of coating the device of Song, Klokkers-Bethke, Talalay and Graf, when the solution is an acid aqueous solution

(preferably pH 4 – 6) because Kohnert teaches that said pH ranges prevent the precipitation of the bone morphogenic member protein (BMP) family member, GDF-5, from solution and insures the device achieves a homogeneous coating (page 7, paragraph 3 and 4) as nonhomogeneous coatings can lead to decreased osteoinductive properties (page 6, 2nd paragraph). Therefore, Kohnert provides specific motivation to optimize the nature of the coating solution (from an organic solvent to an aqueous acidic solution at pH 4 – 6) of Song by teaching that the protein-derived therapeutic agents taught by Song, which include BMP protein (Song, p [0033]), will remain dissolved in aqueous solution at pH 4 – 6.

One would have been motivated to modify the method of coating a medical device rendered obvious by the combination of Song, Klokkers-Bethke, Talalay and Graff with a bioresorbable material such as calcium phosphate and β-tricalcium phosphate because Kohnert teaches that said materials are effective bone-replacement materials (page 1, paragraph 2) and thus are art-recognized as components of medical devices.

**Claim 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Song in WO 2005/016399 A1 (priority date: August 11, 2004, published: February 24, 2005) in view of Klokkers-Bethke *et al.* in US Patent 5,335,769, Talalay in US patent 4,063,367 (published: December 20, 1977) and Graff, D.A. in US Patent 5,316,146 (published: May 31, 1994), as applied to Claims 1, 4, 6, 8, 11 – 12, 16 – 17 and 54, and further in view of Lee *et al.* in US patent 5,571,523; published November 5, 1996).**

*This new ground of rejection is necessitated by Applicant's amendment to Claim 1 and the addition of new independent Claim 54.*

As discussed in the 103(a) rejection above, Song in combination with Talalay and Graff renders obvious the method of instant Claim 1. The references render obvious that the solution contacting the medical device comprises an antioxidant (such as BHT, BHA or tocopherol, instant Claim 14), but does not expressly teach methionine as the antioxidant.

Lee teaches a method for inhibiting artherosclerosis by contacting an artery with an apoptosis-inducing amount of an antioxidant (Abstract) in which methionine is a preferred antioxidant (column 1, lines 37 – 43, Claim 7). Lee teaches that one means for locally delivering the antioxidant is by providing (coating) the antioxidant on the surface of a vascular catheter (a medical device) which contact the wall of a blood vessel (column 1, lines 64 – 67).

It would have been *prima facie* obvious to one skilled in the art, at the time the invention was made, to substitute the antioxidant methionine for the antioxidants rendered obvious by the method of Song, Klokkers-Bethke, Talalay and Graff on a coated medical device, such as a stent or catheter. One would have been motivated to do so because Lee teaches that methionine is effective as an antioxidant on a coated medical device.

**Claim 51 is rejected under 35 U.S.C. 103(a) as being unpatentable over Song in WO 2005/016399 A1 (priority date: August 11, 2004, published: February 24, 2005) in view of Klokkers-Bethke *et al.* in US Patent 5,335,769, Talalay in US**

**patent 4,063,367 (published: December 20, 1977) and Graff, D.A. in US Patent 5,316,146 (published: May 31, 1994), as applied to Claims 1, 4, 6, 8, 11 – 12, 16 – 17 and 54,, and further in view of Gao *et al.* in US patent 6,113,993 (published: September 5, 2000).**

*This new ground of rejection is necessitated by Applicant's amendment to Claim 1 and the addition of new independent Claim 54.*

As discussed in the 103(a) rejection above, Song in combination with Klokkers-Bethke, Talalay and Graff render obvious the method of instant Claim 1. The combination of references render obvious a method for coating implantable medical devices in which the coated substrate comprises metal but do not expressly teach a device made of titanium or a titanium alloy as recited in instant Claim 51.

Gao teaches a method of coating an implant with a calcium phosphate compound on a titanium substrate (Abstract). Gao teaches that orthopaedic implants are commonly made of titanium alloy because of its corrosion resistance to body fluids. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made, to adapt the method of coating a medical device made of metal, rendered obvious over Song, Klokkers-Bethke, Talalay and Graff, to a device made of titanium. One would have been motivated to do so because Gao teaches implants are commonly made of titanium alloys to gain the benefit of their corrosion resistance to body fluids.

***Response to Arguments***

Applicant's arguments filed July 19, 2011 with respect to the rejections under 35 U.S.C 103(a) in light of the amendments to Claim 1 and the addition of new Claim 54 have been fully considered but are moot in view of the new ground(s) of rejection. However, as the references cited in the currently rejections under 35 USC 103(a) have been reapplied, for clarity and in the interest of compact prosecution, relevant arguments regarding the Song, Talalay and Graff references made by Applicant in the Remarks filed 7/19/2011 are addressed below.

Applicant argues that Song describes "dipping techniques," and a person of ordinary skill in the art would interpret "dipping techniques" consistent with the usual dictionary definition of "dip," which is to plunge briefly into a liquid, as in order to wet, coat, or saturate and that independent claim 1 requires "starting isothermal drying of the device while the device remains within the solution held within the receptacle of the container, thereby removing volatile components from the solution of the coating substance." Applicants submit that the Office is reinterpreting the word "dipping" in Song to mean "immersing;" i.e., "while the device remains within the solution held within the receptacle of the container," however, this limitation is simply not described in Song.

This argument is not found to be persuasive for the following reasons. First, the currently applied rejection (as well as the Office Action mailed 4/20/2011) clearly states that "Song teaches the step of drying (i.e. removing volatile components from) a coated medical device in an oven but does not expressly teach the process of isothermal drying as recited in instant Claim 1, step (d). Accordingly, the record is clear that Song does not teach the elements of method step (d) recited in instant Claim 1.

Second, the term "immersing" is not recited in the pending claims and nowhere in the Office Action (mailed 4/20/2011) to which Applicant appears to refer, is the word "immersing" used to describe the dipping method of Song. As discussed in the currently applied 103(a) rejection, the step of starting isothermal drying while the device remains in the coating solution in the container is rendered obvious over Song in view of Klokkers-Bethke, Talalay and Graf for the reasons outlined above.

Finally, it is also pointed out that the currently applied 103 rejection of independent Claim 1 relies on the combination of Klokkers-Bethke *et al.* (a reference not applied in the previous Office Action) and Talalay, not Song and Talalay, to render obvious the limitations of amended independent Claim 1, dependent Claim 11 and new independent Claim 54 drawn to "wherein the inner surface of the receptacle is coated with an inert, repelling material", "starting isothermal drying of the device while the device is held within the (coating) solution within the receptacle to remove volatile components from the solution of the coating substance" and "wherein the container becomes a packaging container for the device".

As explained in the currently applied 103(a) rejection (above), although Song does not teach method step (d) in Claim 1 "starting isothermal drying of the device while the device is held within the (coating) solution within the receptacle to remove volatile components from the solution of the coating substance" and "wherein the container becomes a packaging container for the device" (Claims 11 and 54), Song explicitly teaches the desirability of limiting exposure of the coated medical device to an oxidizing atmosphere by maintaining it in an inert atmosphere and encourages transferring the

coated device to packaging under an inert atmosphere. Accordingly, modifying the drying (dipping) step of Song such that the solvent is removed while the device remains in the coating solution and wherein receptacle becomes the packaging container by applying the freeze drying and package sealing steps of Klokkers-Bethke, both of which are carried out under vacuum and in a nitrogen atmosphere, would limit exposure to an oxidizing atmosphere during solvent removal and, in addition, avoid the need to transfer the coated device from an oxidizing atmosphere to a "package" that contains an inert atmosphere.

Applicant argues that "Talalay does not, for example, describe a device at all. Talalay only describes a method for rapidly drying liquid-solid composites and biologically active materials in situ in a container". Applicant argues that the "packaging container/container [container/receptacle?] can only be provided by Talalay" and that the container used to dip the device of Song into can never be the packaging container (Remarks, page 10).

This argument is not fond to be persuasive because, the currently applied 103(a) rejection, necessitated by amendment to Claim 1 and new Claim 54, relies on the combination of Song and Klokkers-Bethke to render obvious the receptacle becoming the packaging container.

Further, the Examiner acknowledges that Talalay does not describe a device. The Talalay reference, as currently applied, provides motivation to modify the solvent removal method rendered obvious by Song in combination with Klokkers-Bethke (freeze-drying) with isothermal drying.

Applicants argues that "Talalay specifically teaches away from the present invention by expressly requiring that its dried material be well adhered to the container. This is in direct contrast to the feature recited in independent claim 1 that "an inner surface of the receptacle [be] coated with a layer of an inert, repelling material configured to increase a quantitative deposition of the coating substance on the device" (Remarks, pages 9 – 10, bridging paragraph).

In response, the Examiner notes that arguments drawn to Talalay requiring adherence of material to the walls of a container are rendered moot by the new ground of rejection wherein Klokkers-Bethke is applied to address the limitation in amended Claim 1 "an inner surface of the receptacle coated with a layer of an inert, repelling material configured to increase a quantitative deposition of the coating substance on the device"

***Conclusion***

Claims 1, 4, 6, 8 – 9, 11 – 17, 48 and 51 – 54 are rejected. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DENNIS HEYER whose telephone number is (571)270-7677. The examiner can normally be reached on Monday-Friday 8AM-5PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, BRANDON FETTEROLF can be reached at (571)272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/DENNIS HEYER/
Examiner, Art Unit 1628

/Timothy P Thomas/
Primary Examiner, Art Unit 1628